

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ISPH-0377	FOR FURTHER ACTION		ication of Transmittal of International Examination Report (Form PCT/IPEA/416)
International application No.	International filing date (day/n	nonth/year)	Priority date (day/month/year)
PCT/US99/16219	19 JULY 1999		25 SEPTEMBER 1998
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.			
Applicant ISIS PHARMACEUTICALS, INC.			
<ol> <li>This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</li> <li>This REPORT consists of a total of sheets.</li> </ol>			
This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).			
These annexes consist of a total of sheets.			
3. This report contains indications relating to the following items:			
I X Basis of the report			
II Priority			
III Non-establishment of report with regard to novelty, inventive step or industrial applicability			
IV Lack of unity of invention			
V X Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement			
VI Certain documents cited			
VII Certain defects in the international application			
VIII Certain observations on the international application			
Date of submission of the demand	Date	of completion	of this report
18 APRIL 2000	29	JULY 2000	
Name and mailing address of the IPEA/U		orized officer	10
Commissioner of Patents and Tradem. Box PCT Washington, D.C. 20231		NDREW WA	NG (1)
Facsimile No. (703) 305-3230	Telep	hone No. (	703) 308-1235

Form PCT/IPEA/409 (cover sheet) (July 1998)★



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/16219

		<del></del>		
	SIFICATION OF SUBJECT MATTER			
IPC(6) :CO7H 21/04: A61K 48/00: C12Q 1/68: C12N 15/85 US CL : 435/6, 325, 366: 514/44: 536/23.1, 24.5				
According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS	S SEARCHED			
Minimum doc	umentation searched (classification system follower	ed by classification symbols)		
U.S. : 43:	5/6, 325, 366; 514/44; 536/23.1, 24.5			
Documentation NONE	Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched			
•	NOTE:			
Electronic data	a base consulted during the international search (n	ame of data base and, where practicable,	search terms used)	
	INE, EMBASE, SCISEARCH, CAPLUS, BIOSIS			
			· · · · · · · · · · · · · · · · · · ·	
C. DOCUM	SIENTS CONSIDERED TO BE RELEVANT		j	
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.	
	GEWIRTZ et al. Facilitating oligon		1-18	
	entisense deliver on its promise. Proc.			
1	Vol. 93, pages 3161-3163, see entire of	locument.		
	BRANCH. A good antisense molec February 1998. Vol. 23, pages 45-50,		1-18	
1	cordary 1998. Vol. 23, pages 43-30,	see entire document		
		• '		
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		·		
1				
	documents are listed in the continuation of Box C			
	categories of cited documents: ent defining the general state of the art which is not considered	"T" later document published after the inter date and not in conflict with the applicat	tion but cited to understand the	
to be of	f particular relevance	principle or theory underlying the inver		
	document published on or after the international filing date	"N" document of particular relevance; the considered novel or cannot be considered		
cited to	ent which may throw doubts on priority claim(s) or which is a stablish the publication date of another citation or other	"Y" document of particular relevance: the	4.5 4.5	
	reason (as specified) ent referring to an oral disclosure, use, exhibition or other means	considered to involve an inventive	step when the document is	
	ent published prior to the international filing date but later than	combined with one or more other such being obvious to a person skilled in the		
	orty date claimed	"&" document member of the same patent to	family	
Date of the actu	ual completion of the international search	Date of mailing of the international sear	ch report	
10 SEPTEME	3ER 1999	<b>29</b> NOV 1999	, _	
	ing address of the ISA US	Authorized officer 'MAIA	1011-2	
Box PCT	of Patents and Trademarks	ANDREW WANG	10x 1	
Washington, D. Facsimile No.	.C. 20231 (703) 305-3230	Telephone No. (703) 308-0196	( )	
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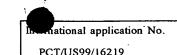


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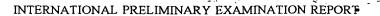
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I	ational application No.	
1 _		

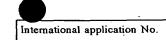
I. I	Basis o	f the report	
1 Wi	th regan	to the elements of the international application	on:*
x	<b>-</b> -	nternational application as originally fi	
		lescription:	
X	1	s1-53	, as originally filed
		s NONE	, filed with the demand
			, filed with the letter of
X	j	laims:	
		s 54-55 s NONE	, as originally filed
		·	, as amended (together with any statement) under Article 19
		Y	vith the letter of, filed with the demand
	P-8-	, , , ,	
x	the d	rawings:	·
	page	NONE NONE	, as originally filed
	page	s NONE	, filed with the demand
	page	NONE NONE	, filed with the letter of
Γ <del>υ</del>	1 44		
X		equence listing part of the description:  s1-11	, as originally filed
			, as originally fried , filed with the demand
	page	NONE	, filed with the letter of
	the la	inguage of publication of the internation	he purposes of international search (under Rule 23.1(b)).  nal application (under Rule 48.3(b)).  purposes of international preliminary examination (under Rules 55.2 and
	ith rega		sequence disclosed in the international application, the international asis of the sequence listing:
x	ł		•
_		ined in the international application in	
X		together with the international applicat	•
F		shed subsequently to this Authority in	
	!	shed subsequently to this Authority in o	
<u> </u>	The s	tatement that the subsequently furnished ational application as filed has been furn	written sequence listing does not go beyond the disclosure in the aished.
		tatement that the information recorded in continuous	omputer readable form is identical to the writen sequence listing has
4. X	The	amendments have resulted in the cance	ellation of:
	X	the description, pagesNONE	
	X	the claims, Nos. NONE	<del></del>
	x	the drawings, sheets/fig NONE	
5.	This	· · · · · · · · · · · · · · · · · · ·	mendments had not been made, since they have been considered to go
in	beyo blacementhis rep	and the disclosure as filed, as indicated in that sheets which have been furnished to the recort as "originally filed" and are not annex	
	1 70.17, v renla		must be referred to under item 1 and annexed to this report.





Reasoned statement under Article 3 citations and explanations supporting	ng such statem	ent	ustriai applicability
statement		,	
Novelty (N)	Claims	1-18	
	Claims	NONE	N
Inventive Step (IS)	Claims	1-18	Y
	Claims	NONE	N
Industrial Applicability (IA)	Claims	1-18	Ү
industrial Applicatinity (IA)	Claims	NONE	N
	Claims		<u> </u>
antisense oligos. Claims 1-18 meet the criteria set out in PC	T Article 33(4), f	or industrial applicability.	
NEW CITATIONS	<del></del>		
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Supplemental Box	Supp	lemental	Box
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(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

#### CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(7): C07H 21/04; A61K 48/00; C12Q 1/68; C12N 15/85 and US Cl.: 435/6, 325, 366; 514/44; 536/23.1, 24.5